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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/907,041	08/06/1997	JOEL S. GREENBERGER	76333/103	7766

7590 07/02/2004

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/907,041	GREENBERGER, JOEL S.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and reply, and declaration by Dr. Anatoly Dritschilo filed 5-17-04 have been entered. Claims 1-32 are pending and under consideration.

Terminal Disclaimer

1. The terminal disclaimer filed on 7-24-02 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent 5,599,712 has been reviewed and is accepted. The terminal disclaimer has been recorded.

2. The terminal disclaimer filed on 5-17-04 is improper. The application/patent being disclaimed has been improperly identified since the number used to identify the US Patent 6,211,848 being disclaimed is incorrect. The correct number is US Patent 6,221,848.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-26 and 30-32 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No.

6,221,848 ('848). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof, and is repeated for the reasons set forth in the preceding Official action mailed 12-15-03. The submitted terminal disclaimer filed 5-17-04 is improper as discussed above under "Terminal Disclaimer" section and the claims remain rejected for the reasons of record.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the pharmaceutically acceptable vehicle is selected from the group consisting of a liposome, an adenovirus vector and a ligand-DNA conjugate" in claim 29 is vague and renders the claim indefinite. The specification states "[I]n this context a pharmaceutically acceptable vehicle can be a solid, liquid or gaseous material that can be used as a vehicle for administering a medicament because the material is inert or otherwise medically acdeptable, as well as compatible with the active agent...a pharmaceutically acceptable carrier can contain conventional additives like diluents, adjuvants, antioxidants...More particularly, pharmaceutically acceptable vehicles are characterized by having physiologically acceptab le pH and ionic strength. Sterile, buffered saline, particularly phosphate-buffered saline, is a preferred

vehicle for compositions." (e.g. see specification , p. 10). The pharmaceutically acceptable vehicle appears to be an inert material, such as a buffered saline, however, an adenovirus vector or a ligand-DNA complex is not an inert material. It is unclear as to the metes and bounds of what would be considered "pharmaceutically acceptable vehicle". If an adenovirus vector or a ligand-DNA complex is a pharmaceutically acceptable vehicle, then it is unclear whether the polynucleotide in claim 27 is within the adenovirus vector or ligand-DNA complex, or said polynucleotide is separated from said adenovirus vector or ligand-DNA complex.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartman et al., 1988 (EP 0284105) in view of Gregory et al., 1997 (US Patent 5,670,488A).

Claims 27-29 are directed to a pharmaceutical composition comprising a polynucleotide that encodes a protein that is capable of neutralizing or eliminating toxic species, such as a free radical, a superoxide anion, or a heavy metal, and a pharmaceutically acceptable vehicle for said polynucleotide. Claim 28 specifies the polynucleotide encodes a gamma glutamyl transpeptidase (gamma-GTP), a manganese superoxide dismutase (Mn-SOD), or a metallothionein (MT). Claim 29 specifies the pharmaceutically acceptable vehicle is a liposome, an adenovirus vector, or a ligand-DNA conjugate.

Hartman teaches construction of a plasmid pMSE-4 containing a human manganese superoxide dismutase (hMnSOD) coding region under the control of lamda P_L promoter, and use of said plasmid to transfect E. coli cells for producing recombinant hMnSOD. The method of preparing the plasmid DNA is as described in Maniatis (e.g. p. 16, Example 2). The common buffer solution for the plasmid DNA described in Maniatis is TE buffer. Hartman also teaches a pharmaceutical composition comprising the human manganese superoxide dismutase or its analog in a suitable pharmaceutical carrier and use of said pharmaceutical composition to treat a subject suffering from a disorder associated with the generation of oxygen free radicals sufficient to cause undesirable symptoms (e.g. p. 14).

Hartman does not teach administering an adenovirus vector expressing superoxide dismutase to a subject.

Gregory teaches using an adenovirus vector Ad2/CFTR-1 or pseudo-adenovirus vectors (PAVs) comprising DNA sequence encoding CFTR and DNA sequence encoding antioxidants, such as superoxide dismutase, for gene therapy in vivo (e.g. column 11, 12). Gregory teaches using TBS solution as a carrier for adenovirus vector for gene transfer in vivo (e.g. column 31).

It would have been obvious for one of ordinary skill at the time of the invention to substitute the plasmid or the human manganese superoxide dismutase as taught by Hartman with the adenovirus vector as taught by Gregory because gene therapy in vivo was known in the art and Gregory teaches using adenovirus vector expressing CFTR and superoxide dismutase, which encompasses manganese superoxide dismutase, for gene transfer in vivo. Although the buffer solution containing the plasmid DNA as taught by Hartman is TE buffer, it would have been obvious for one of ordinary skill to use suitable pharmaceutical carrier for gene transfer in vivo

because Hartman teaches using a pharmaceutical composition comprising a human manganese superoxide dismutase for treating a subject and Gregory teaches using TBS solution as a pharmaceutical carrier for gene transfer in vivo.

One having ordinary skill in the art at the time the invention was made would have motivated to do so in order to use the adenovirus vector as a gene therapy vehicle for treating cystic fibrosis in a subject as taught by Gregory with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER